

IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE

ROQUETTE FRÈRES, )  
Plaintiff, )  
v. ) C.A. No. 06-540 (GMS)  
SPI PHARMA, INC. and DRYTEC LTD., )  
Defendants. )

**PLAINTIFF'S SUR-REPLY BRIEF IN OPPOSITION  
TO DEFENDANT'S MOTION FOR LEAVE  
TO AMEND ITS ANSWER, DEFENSES AND COUNTERCLAIMS**

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## ARGUMENT

### I. SPI'S INTERPRETATION OF JP 61-85331 AND JP 61-85330 IS PLAINLY INCORRECT

SPI does not refute Roquette's demonstration that SPI in its opening brief misrepresented the content of two Japanese prior art references, JP 61-85331 and JP 61-85330, by erroneously stating that those references showed data that they in fact do not show. Instead, SPI now proposes a new "interpretation" of the data reported in those references, namely that "% 200mesh th" means the percentage of particles retained on a 200 mesh sieve, rather than the percentage passing through (SPI Reply Br. at pp 7-9).

Surprisingly, in view of SPI's tacit admission that its motion misrepresented crucial data, SPI's newly proposed interpretation again misrepresents the content of the two Japanese references.

The first three columns of Table I from JP 61-85331, as they appear in that document, are reproduced below.

表 I 物性値

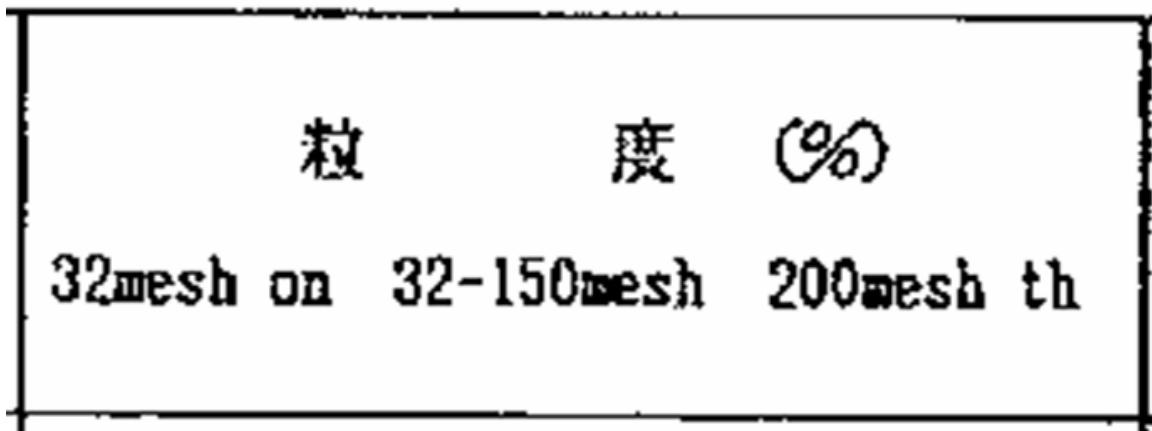
| 物性<br>試料 | 嵩比容<br>(ml/g) | 粒 度 (%)   |            |            |
|----------|---------------|-----------|------------|------------|
|          |               | 32mesh on | 32-150mesh | 200mesh th |
| 実施例 1    | 1.91          | 0         | 26         | 69         |
| " 2      | 2.36          | 0         | 21         | 73         |
| " 3      | 2.08          | 1         | 86         | 9          |
| " 4      | 2.13          | 1         | 91         | 4          |
| 参考例 1    | 1.76          | 0         | 8          | 84         |
| " 2      | 1.91          | 0         | 5          | 89         |
| " 3      | 1.93          | 3         | 92         | 1          |
| 参考例 4    | 1.68          | 0         | 11         | 89         |

As explained in Roquette's Answering Brief, the heading "200mesh th" refers to the percentage of particles that passed through a 200mesh (75 micron) sieve, that is, those particles which were smaller than 75 microns in size. The heading "32mesh on" explicitly refers to the percentage of particles that were retained on a 32mesh sieve. Finally, the heading "32-150mesh" refers to the percentage of particles between those mesh sizes, that is, those particles that passed through the 32mesh sieve and were retained on a 150mesh sieve.

According to SPI, the right-most column heading instead reads "200mesh tb" and, without offering any explanation of what "tb" might mean, SPI contends that this heading represents the percentage of particles retained on a 200 mesh sieve.

SPI's translation and interpretation of Table I are demonstrably incorrect.

The relevant column headings of Table I are reproduced in expanded view below.<sup>1</sup>



Plainly, the text following "200mesh" reads "th" and not tb as SPI contends.

<sup>1</sup> Roquette obtained a copy of JP 61-85331 (as well as JP 61-85330) from the Japanese Patent Office website, which permits viewing of the document in both normal and expanded view. This pasted image is taken from the expanded view, and is further expanded by 250%.

Moreover, the "200mesh th" heading must be interpreted as meaning something different than the heading "32mesh on," contrary to SPI's strained contention that the labels "on" and "th" should both be interpreted to mean "on." The only possible meaning that can be reasonably assigned to "th" in that context is "through."

Consistent with that plain reading, JP 61-85330 (which was issued to the same Applicant as JP 61-85331) reports data under the same three categories of mesh sizes, and there SPI correctly translates the 200mesh heading as "200 mesh th." (SPI Reply Br., Exh. C at p. 3). Notwithstanding that SPI correctly translates "200 mesh th." in JP 61-85330, it fails to mention that in its Reply Brief. Quite to the contrary, SPI disregards its own English translation and states:

Similarly, the same interpretation is given with respect to the data in Table I of JP 61-85330. (SPI Reply Br. at p. 8).

SPI asserts that the word "through" does not exist in the Japanese documents (SPI Reply Br. at n. 3). However, that assertion also is plainly incorrect and is contradicted by SPI's own English translations. As noted, the heading "32-150mesh" refers in part to particles that have passed through the 32mesh sieve, which SPI does not contest. Moreover, each of SPI's submitted English translations includes at least two occurrences of the word "through" used in the context of describing particles having passed through a specified mesh sieve. (SPI Reply Br., Exh. B at p. 4 (Reference Examples 1 and 3), and Exh. C at p. 3 (Reference Examples 1 and 2)).

In light of SPI's misrepresentations noted in Roquette's Answering Brief, the continued misrepresentation of the content of the Japanese references is a matter of serious concern.

SPI is well aware of, and in fact utilizes in its own course of business, the same methodology of reporting particle sizes by reference to percentage of particles retained "on"

some sieves and percentage of particles that pass "through" other sieves. (See Exh. A, hereto).

As the following excerpt from Exh. A portrays, SPI reported its existing and proposed particle size specifications for Mannogem EZ using the same "retained" and "through" terminology:

|           |                                      |
|-----------|--------------------------------------|
| 250 um    | <b>NMT 5% retained</b>               |
| 75 um     | <b>NLT 74% retained (cumulative)</b> |
| 53 micron | <b>NMT 22% through</b>               |

**The new proposed specifications are:**

|        |                                      |
|--------|--------------------------------------|
| 250 um | <b>NMT 5% retained</b>               |
| 75 um  | <b>NLT 60% retained (cumulative)</b> |
| 45 um  | <b>NMT 11% through</b>               |

As demonstrated, SPI's newly described "interpretation" of the particle size data in each of JP 61-85331 and JP 61-85330 is clearly erroneous. When that data is viewed correctly, it is evident as explained in Roquette's Answering Brief that those Japanese documents report precisely what the '777 patent states that they report. Namely, JP 61-85331 discloses mannitol products that have excessively high levels of particles smaller than 75 microns when starch hydrolysate is low (e.g., less than 5.0%) and have fewer particles of that size when starch hydrolysate is high (e.g., 15% and 25%) but these latter products incur other deficiencies, including excessive hygroscopicity. Similarly, JP 61-85330 discloses mannitals in which more than 50% of the particles have a size of less than 200 mesh (75 microns), again precisely what the '777 patent states.

SPI's statement that JP 61-85331 discloses that any particle size can be obtained on an arbitrary basis as a consequence of the spray drying process (SPI Reply Br. at p. 10) also is incorrect. The sentence which SPI quotes from JP 61-85331 (Reply Br. at p. 10) clearly states that the particle size distribution can be varied "in combination with the concentration of the

aqueous solution or slurry." That is, JP 61-85331 explains what its data in Table I reports and what the '777 patent states, that the particle size of mannitol obtained under the disclosure of that Japanese document varies depending upon the level of starch hydrolysate introduced. Indeed, JP 61-85331 states that observation even more clearly by stating:

However, when the requirements for the additive rate of hydrolyzed starch, state of solution of D-mannitol and hydrolyzed starch, and spray dry conditions are satisfied, D-mannitol/hydrolyzed starch complex particles having compressibility as a direct tableting vehicle can be obtained and the obtained particles can range from fine granules to fine powder and have compressibility on an arbitrary basis. (Roquette Answering Br., Exh. A, English translation of JP 61-85331, at p. 11) (emphasis added).

Thus, JP 61-85331 discloses that the particle size obtained will depend upon the amount of starch hydrolysate introduced. That is precisely what the '777 patent states, which SPI does not contest.

SPI's allegations of inequitable conduct in characterizing the disclosures of JP 61-85331 and JP 61-85330, which allegations in any event would be insufficient to survive a motion to dismiss, are based upon assumptions and interpretations that as demonstrated are plainly incorrect.

When the data labeled "200 mesh th" is correctly viewed as referring to the percentage of particles that passed through a 200 mesh (75 micron) sieve, it is clear that the Japanese references actually disclose what the '777 patent accurately states that they disclose, and SPI's allegation of inequitable conduct based upon the '777 patent's entirely accurate characterization of those Japanese references is devoid of merit.

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II. SPI'S NEW ALLEGATION REGARDING DATA PROVIDED IN EXAMPLE 2 OF THE '777 PATENT ARE WITHOUT MERIT

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SPI raises a new allegation in its Reply Brief that the '777 patent presents misleading data in the Table appearing a columns 11-12, which SPI refers to as "Table 1."

Specifically, SPI alleges that the data under the column headed "Mannitols described in JP 61-85330" is inconsistent because it reports "impossible to measure" for friability and apparent density, which require a 100-200 micron particle size cut, but includes data for dissolution time according to Test II, which Test also requires a 100-200 particle size cut.

However, with a small amount of consideration, it is readily apparent that those data entries make sense. As SPI has repeatedly admitted, the '777 patent states that mannitol obtained according to the procedure described in JP 61-85330 exhibits predominantly particles that are smaller than 75 microns. Accordingly, the friability test and apparent density test as described in detail in the '777 patent, which are necessarily conducted on a sample consisting of 100-200 micron size particles, would have been impossible.

Although the dissolution test (Test II) described in the '777 patent also requires a 100-200 micron cut sample, the dissolution time under that test can be inferred from the dissolution time observed for smaller sized particles as would have been obtained under JP 61-85330.

Common sense dictates that larger particles will require more time to dissolve than smaller particles. Accordingly, the Mannitols described in JP 61-85330 (i.e. particles that are smaller than a 100-200 micron cut) would necessarily have dissolved *faster* than would have been observed if it were possible to obtain a 100-200 micron cut of that product. That is, the dissolution times (40-60 seconds) shown in the '777 patent for those mannitol described in JP 61-85330 would have represented a *minimum* dissolution time. Given that the '777 patent describes, and claims, that the dissolution time observed for mannitol according to the invention was less than about 30 seconds, the observed *minimum* dissolution time of 40-60 seconds for the

smaller sized particles described in JP 61-85330 would have been sufficient to report that data as minimum dissolution times that would be obtained according to Test II.

The fact that Roquette saw fit to include dissolution time data for other mannitol, despite the fact that such other mannitol could not provide the requisite 100-200 micron cut, is testimony to Roquette's intent to disclose its information to the Patent Office – not conceal it.

SPI's new allegation to the contrary is inaccurate, misplaced and without merit.

**III. SPI'S NEW ALLEGATION REGARDING COMPRESSIBILITY DATA NOT PROVIDED IN EXAMPLE 3 OF THE '777 PATENT ALSO IS WITHOUT MERIT**

In its Reply Brief, SPI contends for the first time that Roquette possessed and withheld from the U.S. Patent and Trademark Office some unidentified "compressibility data" for prior art granular mannitol powder that should have been included in the Table appearing in Example 3 of the specification, which Example 3 reports data relating only to hardness of lactose and sucrose tablets.

However, SPI fails to offer any explanation of why compressibility of granular mannitol powder would have been relevant to hardness of lactose or sucrose tablets. The '777 patent explicitly states that Example 3 compares the mannitol according to the disclosed invention with commercial products that were then utilized for tableting, which commercial products were based on lactose or sucrose. Comparison with those products is consistent with the patent's description of the background of the industry that;

The pharmaceutical industry consumes large tonnages of sucrose and lactose. These are especially used as excipients in dry forms which are, for example, . . . tablets. ('777 patent at Col. 1, lines 13-18) (emphasis added).

Thus, whereas the '777 patent provides comprehensive data comparing the invention with other mannitol products in Example 2, the data disclosed in Example 3 was for

the clear and stated purpose of further comparing the invention with known products other than mannitol – namely, lactose and sucrose tablets.

SPI's contention that Example 3 should have included comparative data with other mannitol products simply misses or ignores the stated purpose of that Example.

SPI's continued misrepresentation of the content of two Japanese references, which is exacerbated by the facts that SPI presented its initial faulty characterizations without providing English translations and now presents its new, and again faulty, interpretation in apparent disregard of its now-submitted English translations, is cause for concern and, in any event, a clearly inadequate basis for its proposed new inequitable conduct claims.

SPI presents in its Reply Brief new theories and allegations that it did not even raise in its Motion, which original motion itself was untimely and unduly delayed. To base its evolving allegations of inequitable conduct on such shifting sands is fundamentally inconsistent with Rule 9(b)'s requirement that such claims be pled with particularity and Rule 16(b)(4)'s prohibition against modifying the Scheduling Order absent good cause.

Roquette repeats that SPI has failed to allege any valid reason to permit amendment, and that amendment under the present circumstances would be futile and inconsistent with the interest of justice. Finally, both SPI's opening brief and its reply are devoid of any evidence of any intent to deceive which is a necessary element of inequitable conduct.

### CONCLUSION

For the foregoing reasons, Roquette submits that SPI's motion for leave to amend its pleadings to include inequitable conduct allegations should be denied.

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February 6, 2008  
1479897

**CERTIFICATE OF SERVICE**

I, the undersigned, hereby certify that on February 6, 2008, I electronically filed the foregoing with the Clerk of the Court using CM/ECF which will send notification of such filing to the following:

John W. Shaw  
Young, Conaway, Stargatt & Taylor

Additionally, I hereby certify that true and correct copies of the foregoing were caused to be served on February 6, 2008 upon the following individuals in the manner indicated:

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## **EXHIBIT A**

# CONFIDENTIAL EXHIBIT